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Chloroxylenol
Interim Registration Review Decision
Case Number 3045

September 2018

Approved by: _____

Anita Pease
Acting Director
Antimicrobials Division

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I. Introduction

This document is the Environmental Protection Agency's (EPA or the Agency) *Interim Registration Review Decision* (ID) for chloroxylenol and is being issued pursuant to 40 CFR sections 155.56 and 155.58. A registration review decision is the Agency's determination whether a pesticide meets, or does not meet, the standard for registration in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The Agency may issue, when it determines it to be appropriate, an interim registration review decision before completing a registration review. Among other things, the interim registration review decision may: 1) require new risk mitigation measures; 2) impose interim risk mitigation measures; 3) identify additional data or other information required to complete the review; and 4) include schedules for submitting the required data, conducting the new risk assessment, and completing the registration review. For further information on chloroxylenol, additional documents can be found in EPA's public docket (EPA-HQ-OPP-2009-0010) at www.regulations.gov.

FIFRA, as amended by the Food Quality Protection Act (FQPA) of 1996, mandated the continuous review of existing pesticides. All pesticides distributed or sold in the United States generally must be registered by the EPA based on scientific data showing that they will not cause unreasonable risks to human health or to the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess and reduce risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically re-evaluates pesticides to make sure that as these changes occur, products in the marketplace can continue to be used safely. Information on this program is provided at http://www.epa.gov/pesticide-reevaluation. In 2006, the Agency implemented the registration review program pursuant to FIFRA section 3(g) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration.

EPA is issuing an interim registration review decision, which includes risk mitigation for chloroxylenol, so that it can move forward with aspects of the registration review that are complete. EPA determined that no pollinator exposure and effects data are necessary to make a final registration review decision for chloroxylenol. The Agency has made a "no effect" determination under the Endangered Species Act (ESA) for chloroxylenol antimicrobial uses for all listed species and designated critical habitat for such species and has therefore concluded that consultation with the Fish and Wildlife Service and the National Marine Fisheries Service under ESA section 7(a)(2) is not required. In addition, the Agency will complete endocrine screening for chloroxylenol, pursuant to the Federal Food, Drug, and Cosmetic Act (FFDCA) 408(p), before completing this registration review. See Appendices C and D, respectively, for additional information on the endangered species assessment and the endocrine screening for the registration review of chloroxylenol.

Summary of Chloroxylenol Registration Review

Chloroxylenol (also known as 4-chloro-3,5-xylenol or p-Chloro-m-xylenol [PCMX]) is an antimicrobial pesticide with a product registered for use as a preservative for the control of bacteria, fungi, and mold in aqueous preparations containing gelatin, solution polymers, and latexes used in the manufacture of medical imaging film, industrial film, scientific film (electron micrographic films, autoradiographic films, autoradiography) and film based diagnostic reagents. There is currently only one registered chloroxylenol (PC Code 086801) pesticide product, and it is formulated as a soluble concentrate. Chloroxylenol products were first registered as pesticides in 1959, and a Reregistration Eligibility Decision (RED) was completed for the chloroxylenol chemical case in September 1994.

This document is organized in five sections: the *Introduction,* which includes this summary and a summary of any public comments and EPA's responses; *Use and Usage*, which describes how and why chloroxylenol is used and summarizes data on its use; *Scientific Assessments*, which summarizes EPA's risk and benefits assessments, any revisions to previous risk assessments, and risk conclusions; the *Interim Registration Review Decision*, which describes the mitigation measures required to address risks of concern and the regulatory rationale for EPA's interim registration review decision; and, last, the *Next Steps and Timeline* for completion of this registration review.

Pursuant to 40 CFR section 155.50, EPA formally initiated registration review for the chloroxylenol chemical case (case 3045) in 2009. The following highlights significant events that have occurred during the registration review of chloroxylenol and can be found in EPA's public docket, EPA-HQ-OPP-2009-0010, accessed at www.regulations.gov:

- March 2009 - Publication of the *Chloroxylenol Summary Document: Registration Review Preliminary Work Plan* for a 60-day public comment period. The Summary Document included the Preliminary Work Plan (PWP) and was accompanied by the: *Summary of Human Health Effects Data for the Chloroxylenol Registration Review Decision Document* and *Summary of Product Chemistry, Environmental Fate, and Ecotoxicity Data for the Chloroxylenol Registration Review Decision Document*.

- September 2009 - Publication of the *Chloroxylenol Final Work Plan* (FWP). No comments were received during the PWP 60-day comment period. There was no change in data needs, planned risk assessments, or the timeline for the chloroxylenol registration review; thus, the FWP did not modify the PWP.

- May 2012 - Generic Data Call-In (GDCI) for chloroxylenol was issued (GDCI-086801-1075). The GDCI required the following data: Dermal Exposure - Indoor (Guideline Number [GLN] 875.1200, Inhalation Exposure - Indoor (GLN 875.1400), Application Exposure Monitoring Data Reporting (GLN 875.1600), Product Use Information (GLN 875.1700), Sediment and Soil Absorption/Desorption for Parent and Degradates (GLN 835.1230), Soil Column Leaching (GLN 835.1240), Direct Photolysis Rate of Parent and Degradates in Water (GLN 835.2240), Aerobic Aquatic Metabolism (GLN 835.4300), Anaerobic Aquatic Metabolism (GLN 835.4400), Seedling Emergence, Tier II (GLN

850.4225), Aquatic Plant Toxicity Test using *Lemna spp.* Tiers I and II (GLN 850.4400), Algal Toxicity, Tiers 1 and II (GLN 850.5400), Daphnid Chronic Toxicity Test (GLN 850.1300), Mysid Chronic Toxicity Test (GLN 850.1350), Fish Early-Life Stage Toxicity Test (GLN 850.1400), 90-Day Inhalation Toxicity (GLN 870.3465), Activated Sludge Sorption Isotherm (GLN 835.1110), Ready Biodegradability (GLN 835.3110), Modified Activated Sludge Respiration Inhibition (GLN 850.6800), and In Vitro Mammalian Chromosome Aberration Test (GLN 870.5375). The GDCI was satisfied by the cancellation of use sites, as well as the submission of acceptable data and data waiver requests.

- September 2017 - The Agency published the *Registration Review Preliminary Risk Assessment for Chloroxylenol* for a 60-day public comment period. One public comment was received by the Center for Biological Diversity stating that "there is no reasonable expectation for the registered use of chloroxylenol to cause direct or indirect adverse effects to threatened and endangered species, and will not adversely modify or destroy any listed species' critical habitat." This comment agreed with the Agency's "no effect" finding under the Endangered Species Act (ESA), see Appendix C, and did not result in an amendment to the chloroxylenol risk assessment.

- March 2018 - The Agency published the *Chloroxylenol Proposed Interim Registration Review Decision* for a 60-day public comment period. No public comments were received.

- September 2018 - The Agency has completed the *Chloroxylenol Interim Registration Review Decision* and will announce its availability in the Federal Register, docket EPA-HQ-OPP-2009-0010.

II. Use and Usage

When chloroxylenol was registered in 1959, products were registered for use in household and domestic dwellings, laundry equipment, bathroom premises, diaper pails, hospitals and related institutional areas and equipment, human footwear, and in industrial processing water and aqueous systems for the preparation of adhesives/binders, latex paints, polymer emulsions, coatings, and photographic wash tanks. There is currently only one registered product containing chloroxylenol, EPA Registration Number 90963-2 by Ortho-Clinical Diagnostics, Inc. (OCD). The product is registered for use as a preservative for the control of bacteria, fungi, and mold in aqueous preparations containing gelatin, solution polymers, and latexes used in the manufacture of medical imaging film, industrial film, scientific film (electron micrographic films, autoradiographic films, autoradiography) and film based diagnostic reagents. There are no residential uses. The product is packaged as a 98.5% active ingredient (a.i.) powder formulation. According to the *Registration Review Preliminary Risk Assessment for Chloroxylenol*, a total annual quantity of chloroxylenol for film use is approximately 600 kg and fewer than 5 facilities use chloroxylenol products. All other chloroxylenol uses registered in 1959 have been deleted

through an amendment to the registration and label, and the FIFRA Section 6(f) requirements were satisfied (MRID 49479101).[1]

III. Scientific Assessments

A. Human Health Risk

A summary of the Agency's human health risk assessment is presented below in support of the registration review of chloroxylenol. For detailed discussions of all aspects of the human health assessment, see the *Summary of Human Health Effects Data for the Chloroxylenol Registration Review Decision Document* located in the public docket EPA-HQ-OPP-2009-0010 at www.regulations.gov.

1. Summary of Human Health Risks/Risk Characterization

The Agency has determined that there are potential inhalation risks of concern for the occupational use of chloroxylenol. According to the *Summary of Human Health Effects Data for the Chloroxylenol Registration Review Decision Document*, the anticipated exposure pathways for workers are dermal and inhalation during the open pouring of chloroxylenol. No oral exposures are anticipated.

Residential Handler and Post-Application Risks:

There are no residential uses for chloroxylenol. Therefore, there are no residential handler or post-application risks of concern from the use of chloroxylenol.

Occupational Handler Risks:

For occupational exposure, the durations of exposure are expected to be short (1-30 days). Chloroxylenol has low toxicity via the oral (Toxicity Category III), dermal (Toxicity Category III), and inhalation (Toxicity Category IV) routes. Chloroxylenol is also a severe eye irritant (Toxicity Category I), which is mitigated by EPA Reg. No. 90963-2's label language that states "*Wear goggles, face shield or safety glasses*." Also, chloroxylenol is a mild dermal irritant from acute (single) exposure (Toxicity Category III) where the most common effect is irritation and erythema of the skin when applied dermally. Chloroxylenol is not a dermal sensitizer.

The dermal toxicological endpoint of concern for chloroxylenol is dermal irritation, which is mitigated via Personal Protective Equipment (PPE) to limit contact to the skin. EPA Reg. No. 90963-2's label includes the signal word "Danger" and PPE, such as rubber gloves, and instructions to remove contaminated clothing. The use information submitted by the registrant also included photographs of workers wearing long pants and long-sleeved shirts; however, the current label does not specifically state this, thus, label mitigation is discussed in Section IV.

[1] MRID 49479101 Hendrix, H. (2014) Product Use Study for Chloroxylenol. Unpublished study prepared by Ortho-Clinical Diagnostics, Inc. 24p.

Potential inhalation exposure is based on the open pouring of the chloroxylenol powder formulation. Use information submitted by the registrant indicates that the largest single event for the open pouring/transferring of powders occurs for the use of chloroxylenol as a material preservative for MicroSlides for biological specimens (e.g., blood slides). This occurs once every 15 years when workers pour/measure 110 pounds of the powder (98.5% a.i.) from the original shipping container into 2 kg dispensing containers to be used throughout the year. The second highest use raising concern for chloroxylenol inhalation exposure is for workers pouring 55 pounds of the powder once every 6 weeks to make a stock solution. The liquid stock solutions (4 and 10 liter containers) are both open poured and/or metered-in to production. EPA Reg. No. 90963-2's label currently states to *"use chemical fume hood or localized exhaust or dust mask or NIOSH approved respirator when handling dry powder. Wear goggles, face shield or safety glasses and rubber gloves when handling."* No respiratory protection is currently required by the label during the liquid pour; thus, label mitigation is discussed in Section IV.

The inhalation exposure assessment to support waiving the inhalation subchronic toxicity study (TXR No. 0057541) is provided in **Table 1**. EPA's Hazard and Science Policy Council (HASPOC) used a weight of evidence approach and recommended that the subchronic inhalation toxicity study not be required for chloroxylenol at this time due to: 1) the hazard profile of chloroxylenol; 2) the Margins of Exposure (MOEs) for the use of this chemical are no lower than 1,600 and do not exceed the Agency's target MOE of 1,000 for inhalation waivers; and (3) application of PPE, such as the use of a filtering face piece respirator, and use of local exhaust when handling dry powders (as described in Section IV.A.1.).

In addition to exposure to the powder formulation, chloroxylenol has a vapor pressure of 0.1 mm Hg at 20°C, and as a result, there is also the potential for off-gassing. The highest potential for inhalation exposure is expected to be from the open pouring of the 98.5% a.i. powder formulation. The best available inhalation exposure data for the open pouring of powder formulations are from the Antimicrobial Exposure Assessment Task Force II (AEATF II, MRID 49905201).[2] The surrogate exposure data from the AEATF II are designed to be used for chemicals with low vapor pressures, typically lower than the 0.1 mm Hg for chloroxylenol. Therefore, to protect against the vapor phase, MOEs are presented in **Table 1** for a range of PPE and engineering controls.

Table 1- Inhalation MOEs for Open Pouring of Chloroxylenol Powder Formulation

Scenario	Concentration[A]	Amount of Product Applied (Pounds)[B]	Amount Ai Handled - AaiH (lb ai)[C]	Unit Exposure (mg/lb ai)[D]	Inhalation Dose[E] (mg/kg/ day)	Inhalation MOE[F] (Target MOE = 1,000)
Make-up of dispensing containers	98.5% ai	110	108	0.0448 (5x PF)	0.061	1,600
				0.0224 (10x PF)	0.030	3,300
				0.000224 (1000x PF)	0.000303	330,000

[2] MRID 49905201. Rosenheck L. (2016) A Study for Measurement of Potential Dermal and Inhalation Exposure During Manual Pouring of Two Solid Formulations Containing an Antimicrobial. Unpublished study dated April 21, 2016. Sponsored by Hasmukh Shah, Ph.D. task force manager. AEATF II Project ID AEA07. 1100 p.

MicroSlides batch preparation		55	54	0.0448 (5x PF)	0.030	3,300
				0.0224 (10x PF)	0.0152	6,500
				0.000224 (1000x PF)	0.000152	650,000
A. EPA Reg. No. 90963-2. B. MRID No. 49479101. C. Amount of AI Handled (AaiH in lb ai) = (% ai/100) x amount of product applied in pounds D. Inhalation unit exposure source: AEATF II MRID 49905201. Where 5x Protection Factor (PF) is a filtering face piece respirator; 10x PF is a ½ face organic vapor (OV) cartridge with a pre-filter and for particulates in the chemical fume hood; and 1000x PF is either an airline respirator or laboratory chemical fume hood for vapors. E. Inhalation Dose (mg/lb ai) = AaiH (lb ai) x Inhalation unit exposure (mg/lb ai) x 1/80 kg body weight F. Inhalation MOE = (Oral NOAEL (Developmental toxicity study in the rat) 100 mg/kg/day) / Inhalation dose (mg/kg/day); Where Target MOE = 1,000.						

A rat developmental study was used to calculate the inhalation MOE. The no observed adverse effect level (NOAEL) of 100 mg/kg/day from the rat developmental toxicity study was used as the point of departure for calculation of inhalation risk. The study NOAEL of 100 mg/kg/day was based on decreased body weight gain and food consumption observed at the lowest observed adverse effect level (LOAEL) of 500 mg/kg/day. The range of inhalation MOEs for the powder portion of the formulated product presented in **Table 1** show a minimum MOE of 1,600 based on the use of a filtering face piece respirator, i.e., 5x protection factor (PF). Additional mitigation measures are also assessed to capture the uncertainties and limitations of using the AEATF II surrogate exposure data for a higher vapor pressure (VP) chemical such as chloroxylenol (VP = 0.1 mm Hg). As a result, **Table 1** indicates that all MOEs are acceptable; however, there are potential inhalation risks of concern unless appropriate PPE and engineering controls are used, thus, label mitigation is discussed in Section IV.

Occupational Post-Application Risks:

There are no occupational post-application risks of concern for the uses of chloroxylenol.

2. Aggregate Risks

Since there are no registered dietary or residential uses of chloroxylenol, an aggregate assessment was not performed.

3. Cumulative Risks

With respect to cumulative exposure, unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to chloroxylenol and any other substances. Chloroxylenol also does not appear to produce a toxic metabolite via other substances. In 2016, EPA's Office of Pesticide Programs released a guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis.*[3] This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning

[3] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework

with the evaluation of available toxicological information and, if necessary, followed by a risk-based screening approach. This framework supplements the existing guidance documents for establishing common mechanism groups (CMGs)[4] and conducting cumulative risk assessments (CRA).[5] The Agency has utilized this framework for chloroxylenol and determined that the available toxicological data suggest chloroxylenol does not share a similar toxicological profile with other pesticides. Thus, no further cumulative evaluation is necessary for chloroxylenol.

4. Human Health Data Needs

There are currently no outstanding human health data requirements for the registered uses of chloroxylenol.

5. Human Incidents

Based on an Incident Data System (IDS) search conducted from 1992 to June 20, 2017, there are no reported human health incidents for chloroxylenol in the IDS database.

6. Tolerances

EPA has not established tolerances or tolerance exemptions for residues of chloroxylenol in/on food under the Federal Food, Drug, and Cosmetic Act (FFDCA) Section 408. There are no registered dietary or residential antimicrobial uses of chloroxylenol, and therefore, there are no anticipated dietary risks.

Chloroxylenol has been listed as a food contact substance by the US Food and Drug Administration (FDA) under FFDCA Section 409. There are no FDA food contact notifications (FCNs) for chloroxylenol. Chloroxylenol has been cleared for use as a preservative in food packaging adhesives under 21 CFR Section 175.105 (c.) (5); however, there are no EPA registrations which allow this use.

B. Ecological Risk

Environmental exposure to chloroxylenol is expected to be negligible. The registrant, OCD, reported that approximately 600 kg of chloroxylenol are produced per year (MRID 49479101) and that most of the chloroxylenol solution is absorbed into the film.

1. Summary of Ecological Risks/Risk Characterization

Aquatic and Terrestrial Organisms

The *Registration Review Preliminary Risk Assessment for Chloroxylenol* states that chloroxylenol is moderately to highly toxic to aquatic organisms and is practically nontoxic to

[4] *Guidance for Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999)
[5] *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (USEPA, 2002)

birds and mammals. EPA determined that no pollinator exposure and effects data are necessary to make a final registration review decision for chloroxylenol. Due to the extremely low production volume, limited use as a film preservative and disposal methods, exposure to aquatic and terrestrial nontarget organisms is not expected.

2. Ecological Data Needs

There are currently no outstanding ecotoxicity or environmental fate data requirements for the registered uses of chloroxylenol.

3. Ecological Incidents

Based on an Incident Data System (IDS) search conducted from 1992 to June 20, 2017, there are no reported nontarget organism incidents for chloroxylenol in the IDS database.

C. Benefits Assessment

Antimicrobial Use Benefits

The use of chloroxylenol as a preservative for the control of bacteria, fungi, and mold is unique because it is used in the manufacture of medical imaging film, industrial film, scientific film (electron micrographic film, autoradiographic film, autoradiography) and film based diagnostic reagents. This pesticidal use in film provides a niche registered use of chloroxylenol, as other pesticides registered for use as a preservative are not used in film.

IV. Interim Registration Review Decision

A. Risk Mitigation Measures and Regulatory Rationale

In evaluating potential risk mitigation for chloroxylenol, EPA considered the risks, the benefits, and the use patterns of chloroxylenol. As indicated in Appendix C, the Agency has made a "no effect" determination under ESA for chloroxylenol. Label amendments are required for the occupational uses of chloroxylenol product EPA Reg. No. 90963-2 due to occupational dermal and inhalation risks of exposure.

The Agency notes that although chloroxylenol is a severe eye irritant, EPA Reg. No. 90963-2 already requires appropriate PPE mitigation to prevent ocular exposure, as the label states "*Wear goggles, face shield or safety glasses*." In addition, although chloroxylenol is moderately to highly toxic to aquatic organisms, the label already states "*This product is toxic to fish and aquatic organisms*."

1. Human Health Risks

To address the potential for occupational risk from the occupational dermal and inhalation risks of exposure, the Agency discussed and agreed upon risk mitigation with the stakeholders Ortho-

Clinical Diagnostics, Inc. (OCD) and Carestream Health, Inc. The risk mitigation measures require OCD to amend EPA Reg. No. 90963-2's label to add appropriate PPE and engineering controls as discussed below.

Occupational Handlers

Due to the occupational handler dermal and inhalation risks of exposure to chloroxylenol during the open pouring of dry powder to make liquid stock solution, the Agency requires labeling changes to EPA Reg. No. 90963-2 (see Appendices A and B).

EPA Reg. No. 90963-2's label currently states *"use chemical fume hood or localized exhaust or dust mask or NIOSH approved respirator when handling dry powder. Wear goggles, face shield or safety glasses and rubber gloves when handling."*

For dermal exposures, the Agency requires that the registration and label be amended to mitigate the potential for dermal irritation by adding to the label requirements for: chemical resistant gloves, long pants, and long-sleeved shirt or apron with sleeve covers.

For inhalation exposures, the Agency requires that the registration and label be amended to mitigate the potential for inhalation irritation to the chloroxylenol dry powder. The Agency is requiring this mitigation because EPA Reg. No. 90963-2's current label language does not require respiratory protection during the liquid pour scenario. Also, the current label language does not specify the worker exposure scenarios and which mitigation must be used in each scenario. The required mitigation below will address those issues. The following amendments to the registration and label are required.

- During the repackaging of chloroxylenol from shipping containers to dispensing containers, the Agency requires that workers wear a NIOSH approved filtering face piece respirator (i.e., 5x protection factor) with a N95 filter (TC-84A) and that a walk-in chemical fume hood or localized exhaust be used.
- During the process to pre-weigh the chloroxylenol powder and during the open pouring of dry powder to make the liquid stock solution, the Agency requires that workers use a chemical fume hood or localized exhaust.

V. Next Steps and Timeline

A. Interim Registration Review Decision

In accordance with 40 CFR Sections 155.56 and 155.58, the Agency is issuing the *Chloroxylenol Interim Registration Review Decision*. A Federal Register Notice will announce the availability of this Interim Decision. EPA determined that no pollinator exposure and effects data are necessary to make a final registration review decision for chloroxylenol. As indicated in Appendix C, the Agency has made a "no effect" determination under ESA for chloroxylenol, and in Appendix D, the Agency's final registration review decision for chloroxylenol will be dependent upon the result of the Agency's EDSP FFDCA section 408(p) determination.

Amendments to the registration and label are required as discussed herein and set forth in Appendices A and B.

B. Implementation of Mitigation Measures

Once the Interim Registration Review Decision is published in the docket, the chloroxylenol registrant Ortho-Clinical Diagnostics, Inc. will be required to submit an amendment to the registration and label that includes the label changes described in Appendices A and B. The amended registration and label will be required to be submitted to the Agency for review within 60 days following publication of the Interim Registration Review Decision.

VI. Appendices

Appendix A: Summary of Required Actions for Chloroxylenol

Registration Review Case: 3045 **PC Code: 086801** **Chemical Type: Preservative for the control of bacteria, fungi, and mold in aqueous preparations containing gelatin, solution polymers, and latexes used in the manufacture of medical imaging film, industrial film, scientific film (electron micrographic films, autoradiographic films, autoradiography) and film based diagnostic reagents.**					
Affected Population(s)	**Source of Exposure**	**Route of Exposure**	**Duration of Exposure**	**Potential Risk(s) of Concern**	**Required Label Changes**
• Occupational handlers	• Skin contact	• Dermal	• Sub-chronic	• Dermal effects	• Add PPE
• Occupational handlers	• Air	• Inhalation	• Sub-chronic	• Inhalation effects	• Add PPE • Add engineering controls

Appendix B: Required Labeling Changes for Chloroxylenol

Description	Required Amended Label Language	Placement on Label
Dermal Protection for EPA Reg. No. 90963-2	"PERSONAL PROTECTIVE EQUIPMENT: Handlers must wear goggles, face shield or safety glasses, chemical-resistant gloves, long pants, and either a long-sleeved shirt or apron and sleeve covers. When handling dry powder during the pre-weighing process and during the open pouring of dry powder to make the liquid stock solution, use chemical fume hood or localized exhaust. When handling dry powder during the repackaging of chloroxylenol from shipping containers to dispensing containers, use a walk-in chemical fume hood or localized exhaust and a NIOSH approved filtering face piece respirator with a N95 filter (TC-84A). You may also use other NIOSH approved particulate respirators that offer more protection such as: • Half face respirator with a N95 filter (TC-84A) • Full face respirator with a N99 filter (TC-84A) • Powered air purifying respirator with an HE filter (TC-21C)"	Precautionary Statements under the heading "Hazards to Humans and Domestic Animals"

Appendix C: Endangered Species Assessment

The *Registration Review Preliminary Risk Assessment for Chloroxylenol* states that the Agency has made a "no effect" determination under the Endangered Species Act (ESA) for chloroxylenol antimicrobial uses for all listed species and designated critical habitat for such species. Therefore, the Agency has concluded that consultation with the Fish and Wildlife Service and the National Marine Fisheries Service under ESA section 7(a)(2) is not required. Unless public comments provide new information or data that warrant such assessment, no additional environmental risk assessment is needed in support of this registration review.

Appendix D: Endocrine Disruptor Screening Program

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its most recent registration decision for chloroxylenol, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), chloroxylenol is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. The Agency has reviewed all of the assay data received for the List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets. A second list of chemicals identified for EDSP screening was published on June 14, 2013[6] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors. Chloroxylenol is not on either list. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[7]

In this interim decision, EPA is making no human health or environmental safety findings associated with the EDSP screening of chloroxylenol. Before completing the registration review for chloroxylenol, the Agency will make an EDSP FFDCA section 408(p) determination.

[6] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
[7] http://www.epa.gov/endo/